UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Office of Prevention, Pesticides
and
Toxic Substances

HED DOC. NO. 013921

MEMORANDUM 12/20/99

SUBJECT: ***PHOSMET:*** **- REVISED** Report of the Hazard Identification Assessment Review Committee - Intermediate-Term Dermal and Inhalation Exposure Assessments of Greater Than 30-Days.

FROM: Linda L. Taylor, Ph.D.
Reregistration Branch I
Health Effects Division (7509C)

THRU: Jess Rowland, Co-Chair
and
Pauline Wagner, Co-Chair
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

TO: Christina Swartz
Reregistration Branch I
Health Effects Division (7509C)

PC Code: 059201

On November 4, 1999, the Health Effects Division's Hazard Identification Assessment Review Committee [HIARC] re-evaluated the toxicological endpoint selected for the intermediate-term dermal and inhalation exposure risk assessments. **This report amends the previous Hazard ID Committee report [HED Document No. 013604] with respect to the intermediate-term dermal and inhalation risk assessments.**

Committee Members in Attendance

Members present were David Anderson, William Burnam, Pam Hurley, Mike Ioannou, Tina Levine, Susan Makris, Nicole Paquette, Kathleen Raffaele, Jess Rowland (Co-Chair), PV Shah, Pauline Wagner (Co-Chair), and Brenda Tarplee (Executive Secretary).

Data were presented by Linda Taylor of Reregistration Branch I.

Other HED members present at the meeting: Whang Phang, Elizabeth Mendez, and Mike Metzger.

Data Presentation: _____

Linda Taylor
Toxicologist

I. SUMMARY

On November 4, 1999, the Health Effects Division's Hazard Identification Assessment Review Committee [HIARC] re-evaluated the toxicological endpoint for the intermediate-term dermal and inhalation exposure risk assessments. This was necessary because use of the selected study lead to a value that was lower [0.5 mg/kg/day] than the one used for the chronic dietary RfD [NOAEL 1.1 mg/kg/day], due to the need for a MOE of 300.

Previously [HED Document No. 013604], the HIARC selected a LOAEL of 1.5 mg/kg/day established in the subchronic **oral** neurotoxicity study in rats for the intermediate-term dermal and inhalation exposures of > 30 days duration. The endpoint was dose-related decreases in plasma, RBC, whole blood, and brain cholinesterase activity at all dose levels; a NOAEL was not established. With the use of a LOAEL, the MOE for these assessments was 300, which lead to a value [0.5 mg/kg/day] lower than the one used for chronic dietary RfD [1.1 mg/kg/day]. Therefore, the HIARC selected the chronic rat study NOAEL of 1.1 mg/kg/day for the intermediate-term [>30 days] exposure risk assessments. The use of a NOAEL established in a chronic study for intermediate-term exposure scenarios is appropriate because: (1) the same endpoint [cholinesterase inhibition] was observed in both studies in the same species [rat] and (2) the LOAEL of 1.5 mg/kg/day in the 90-day study is comparable to the LOAEL of 1.8 mg/kg/day in the chronic study.

This report amends the previous Hazard ID Committee report [HED Document No. 013604; dated August 4, 1999] of the intermediate-term dermal and inhalation exposure risk assessments of greater than 30 days.

II. SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL 4.5	Cholinesterase inhibition [plasma, RBC, brain] and decreased motor activity	Rat Acute Neurotoxicity
Chronic Dietary non-carcinogenic effects	NOAEL=1.1 (UF=100)	Decreased RBC and serum cholinesterase	Rat Chronic Toxicity/Carcinogenicity
		Chronic RfD = 0.011 mg/kg/day	
Short-Term (Dermal)	dermal NOAEL = 15	brain (females)/plasma (males) cholinesterase inhibition	Rat 21-day dermal toxicity
Intermediate-Term (Dermal <**30 days**)	dermal NOAEL = 15	brain (females)/plasma (males) cholinesterase inhibition	Rat 21-day dermal toxicity
Intermediate-Term[1] (Dermal >**30 days**)	oral NOAEL = 1.1	Decreased RBC and serum cholinesterase	Rat Chronic Toxicity/Carcinogenicity
Short-Term (Inhalation)[1]	oral NOAEL 4.5	Cholinesterase inhibition [plasma, RBC, brain] and decreased motor activity	Rat Acute Neurotoxicity
Intermediate-Term (Inhalation <**30 days**)[1]	oral NOAEL = 1.5	brain (females)/plasma (males) cholinesterase inhibition	Rat subchronic neurotoxicity
Intermediate-Term (Inhalation >**30 days**)[1]	oral NOAEL = 1.1	Decreased RBC and serum cholinesterase	Rat Chronic Toxicity/Carcinogenicity
Long-Term (Dermal & Inhalation)	Is not required due to minimal concern for exposure *via* these routes of exposure, based on the use pattern.		

1. appropriate route-to-route extrapolation should be performed for these risk assessments. Exposure values using a dermal absorption factor of 10% should be converted to equivalent oral doses and compared to the oral NOEL.